PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 033388-532	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/00377	International filing date *(day/month/year)* 08 January 2003 (08.01.2003)	Priority date *(day/month/year)* 09 January 2002 (09.01.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 9/127 and US Cl.: 424/450; 264/4.1, 4.3		
Applicant ELAN PHARMACEUTICALS, INC		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 30 July 2003 (30.07.2003)	Date of completion of this report 17 May 2004 (17.05.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer BLESSING FUBARA Telephone No. 571/272-1600

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.
PCT/US03/00377

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-53 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 54-79, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-18, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.
PCT/US03/00377

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-106	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-106	NO
Industrial Applicability (IA)	Claims 1-106	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-7, 9-12, 18-51 and 53-106 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al (US 5,741,513).

GHYCZY et al discloses a method of preparation of liposomes. The method involves dissolving the phospholipid concentrate in ethanol and adding an aqueous medium to prepare a gel and then adding more aqueous medium to prepare the liposomes (col. 3, line 24 through col. 5, line 56 and Examples). What is lacking in GHYCZY et al is the claimed amount of the acidic phospholipid. However, in the absence of showing unexpected results, it is deemed obvious to manipulate the amounts of the acidic phospholipids taught by GHYCZY et al with the expectation of obtaining the best possible product.

Claims 8 and 52 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al cited above, further in view of IGA et al (US 4,877,561).

The teachings of GHYCZY et al have been discussed above. What is lacking in GHYCZY et al is the teaching of the use of acetone as the solvent.

IGA et al while disclosing a liposome gel formulation containing a variety of drugs teach that for the formation of liposome gels, organic solvents such as alcohols and acetone can be used (abstract, col. 1, line 63 through col. 3, line 34).

The use of acetone instead of alcohol taught by GHYCZY et al would have been obvious to one of ordinary skill in the art, since the reference of IGA et al shows that acetone could be used instead of alcohol.

Claims 13-17 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al cited above, further in view of KIRPOTIN et al (US 5,980,935).

The teachings of GHYCZY et al have been discussed above. What is lacking in GHYCZY et al is the teaching of nucleic acids and plasmids as the active agents. The use of nucleic acids and plasmids as the active agents however, would have been obvious to one of ordinary skill in the art since the reference of KIRPOTIN et al shows that these agents are routinely incorporated in liposomes for transfection purposes (note the abstract and examples).

Claims 1-106 meet the criteria set out in PCT Article 33(2) and (4), because the prior art does not specifically teach a method of formation of liposomes using the instant amounts of phospholipids and because the invention finds its utility in the preparation of liposomes and the delivery of a variety of active agents.

---------- NEW CITATIONS ----------

US 4,877,561 A (IGA et al) 31 October 1989 (31.10.1989), see abstract, col. 1, line 63 through col. 3, line 34.

US 5,980,935 A (KIRPOTIN et al) 09 November 1999 (09.11.1999), see abstract and Examples.